Molecular characteristics of Human Endogenous Retrovirus type-W in schizophrenia and bipolar disorder.

Hervé Perron, Nora Hamdani, Raphaël Faucard, Mohamed Lajnef, Stéphane Jamain, Claire Daban-Huard, Samuel Sarrazin, Emmanuel Leguen, Josselin Houenou, Marine Delavest, et al.

SUPPLEMENTARY INFORMATION

Molecular characteristics of Human Endogenous Retrovirus type-W (HERV-W) in schizophrenia and bipolar disorder.

TABLE OF CONTENT:

I. Complementary Statistical analyses:

Table S1: HERV-W RNA relative expression of the MSRV subtype, all controls

Variables	BP,N=91	SZ,N=45	Controls,N=73	P for all	P BP vs TEM	P BP vs SZ	P SZ vs TEM
	Mean(SD)			P value Kruskall Wallis/Mann Whitney			
RNA	1.62 (4.6)	0.84 (0.5)	0.65 (0.6)	<0.0001	<0.0001	0.01	0.012
DNA	0.61(0.3)	0.55(0.3)	0.77(0.3)	0.0005	0.0016	0.575	0.0003

Table S2: HERV-W relative expression of the MSRV subtype,
Controls with negative CRP (C-)

Variables	BP,N=91	SZ,N=45	Controls,N=46	P for all	P BP vs TEM	P BP vs SZ	P SZ vs TEM
	Mean(SD)			P value Kruskall Wallis/Mann Whitney			
RNA	1.62 (4.6)	0.84 (0.5)	0.62 (0.6)	<0.0001	<0.0001	0.01	0.007
DNA	0.60(0.3)	0.55(0.3)	0.77(0.3)	0.0015	0.003	0.575	0.0006

Table S3: HERV_W RNA relative expression and DNA copy numbers of the MSRV subtype.
Statistical analyses excluding Bipolar Disorder Patients treated with Valproate.

Variables	BP,N=68	SZ,N=45	Controls,N=73	P for all	P BP vs TEM	P BP vs SZ	P SZ vs TEM
	Mean(SD)			P value Kruskall Wallis/Mann Whitney			
RNA	1.71 (5.3)	0.84 (0.5)	0.65 (0.6)	<0.0001	<0.0001	0.087	0.007
DNA	0.61(0.3)	0.55(0.3)	0.77(0.3)	0.0009	0.006	0.468	0.0003

II. Sequence analyses

Figure S1: Sequence alignements with the HERV-W/MSRV-env specific Probe

Figure S1A: HC RNA

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MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG
            AAGAAGTTTACCTCGGGGTCTACGTC

1. RNA-H12_1     40        50
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MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

2. RNA-H12_1     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
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MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

3. RNA-H12_1     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
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MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

4. RNA-H12_1     40        50
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MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

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MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

33. RNA-H12_    320       330
[   88 ]    TTCTTCAAATGGAGCCCCAGA--CAG>
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MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG
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Figure S1B: HC DNA

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            AAGAAGTTTACCTCGGGGTCTACGTC

1. DNA-H12_1     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
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3. DNA-H16_1     40        50
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MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG
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Figure S1C: BD RNA

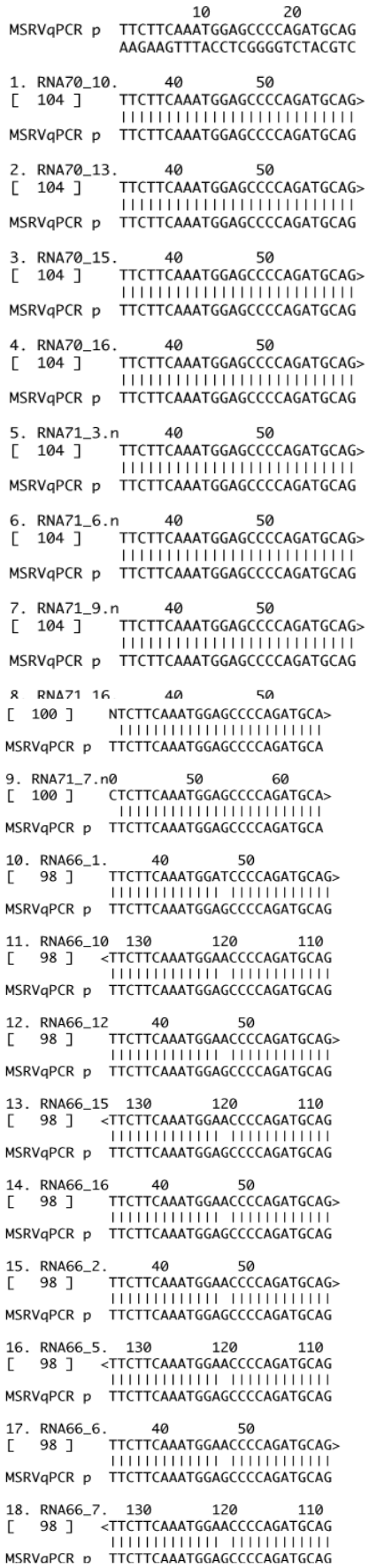

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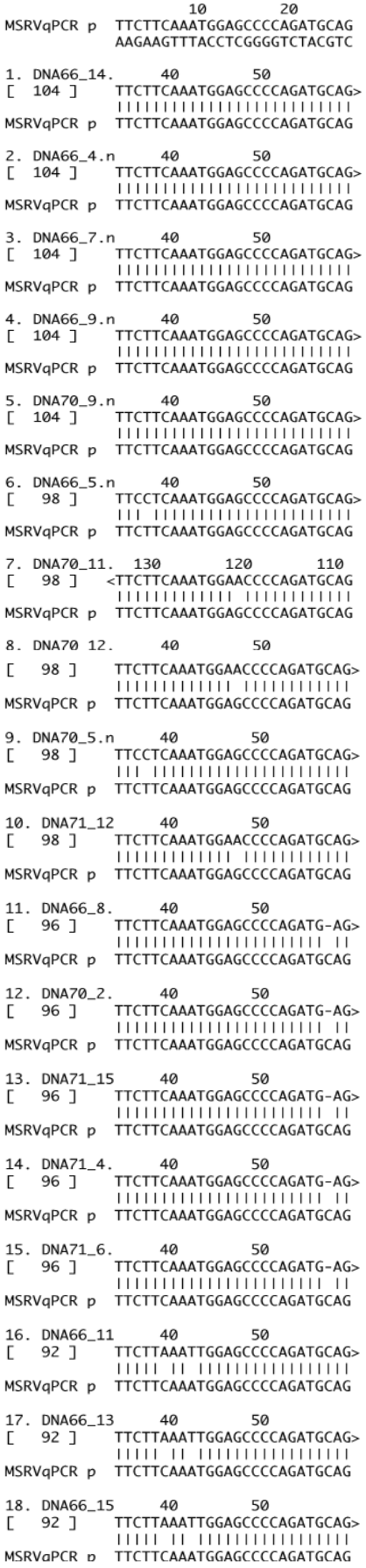
Figure S1D: BD DNA



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             |||||| || ||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

31. DNA71_5.     40        50
[   92 ]    TTCTTAAATTGGAGCCCCAGATGCAG>
             |||||| || ||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

32. DNA71_7.     40        50
[   92 ]    TTCTTAAATTGGAGCCCCAGATGCAG>
             |||||| || ||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

33. DNA71_8.     40        50
[   92 ]    TTCTTAAATTGGAGCCCCAGATGCAG>
             |||||| || ||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG
```

Figure S1E: SZ RNA

```
                    10        20
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG
            AAGAAGTTTACCTCGGGGTCTACGTC

1. RNA11_10.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

2. RNA11_11.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

3. RNA11_12.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

4. RNA11_14.      40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

5. RNA11_15.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

6. RNA11_2.n     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

7. RNA11_3.n     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

8. RNA11 6.n     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

9. RNA11_8.n     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

10. RNA11_9.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

11. RNA16_10     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

12. RNA16_2.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

13. RNA16_3.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

14. RNA16_9.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

15. RNA23_12     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

16. RNA23_16     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

17. RNA23_2.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

18. RNA23_4.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
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MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG
```

```
19. RNA23_6.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
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MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

20. RNA23_9.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

21. RNA32_10     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

22. RNA32_11     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

23. RNA32_12     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

24. RNA32_13     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

25. RNA32_14     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

26. RNA32_16     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

27. RNA32_3.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

28. RNA32_4.  130       120       110
[  104 ]   <TTCTTCAAATGGAGCCCCAGATGCAG
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

29. RNA32_5.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

30. RNA32_7.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

31. RNA32_8.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

32. RNA32_9.     40        50
[  104 ]    TTCTTCAAATGGAGCCCCAGATGCAG>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

33. RNA23_10     40        50
[  100 ]    TTCTTCAAATGGAGCCCCAGATGCA>
            ||||||||||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCA

34. RNA11_16     40        50
[   98 ]    TTCTTCAAATGGAGCCCCAGAGGCAG>
            |||||||||||||||||||| ||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

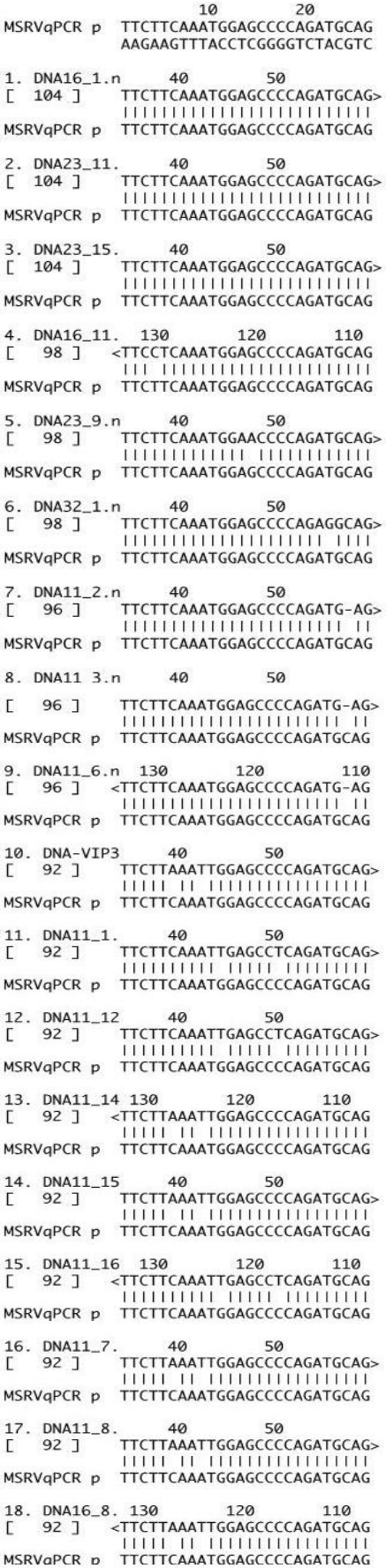
35. RNA11_4.     40        50
[   98 ]    TTCTTCAAATGGAGCCCCAGAGGCAG>
            |||||||||||||||||||| ||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

36. RNA23_3.     40        50
[   98 ]    TTCTTCAAATGGAGCTCCAGATGCAG>
            |||||||||||||| ||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

37. RNA23_5.     40        50
[   98 ]    TTCTTCAAATGGAGCCCCAGAGGCAG>
            |||||||||||||||||||| ||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

38. RNA16_11     40        50
[   88 ]    TTCTTCAAATGGAGCCCCAGA--CAG>
            ||||||||||||||||||||  |||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG
```

Figure S1F: SZ DNA



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19. DNA23_14     40        50
[   92 ]    TTCTTCAAATTGAGCCTCAGATGCAG>
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MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

20. DNA23_2. 130       120       110
[   92 ]   <TTCTTAAATTGGAGCCCCAGATGCAG
            ||||| || ||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

21. DNA23_4.     40        50
[   92 ]    TTCTTAAATTGGAGCCCCAGATGCAG>
            ||||| || ||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

22. DNA23_8. 130       120       110
[   92 ]   <TTCTTAAATTGGAGCCCCAGATGCAG
            ||||| || ||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

23. DNA32_12     40        50
[   92 ]    TTCTTAAATTGGAGCCCCAGATGCAG>
            ||||| || ||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

24. DNA32_15 130       120       110
[   92 ]   <TTCTTAAATTGGAGCCCCAGATGCAG
            ||||| || ||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

25. DNA32_2.     40        50
[   92 ]    TTCTTAAATTGGAGCCCCAGATGCAG>
            ||||| || ||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

26. DNA32_3.     40        50
[   92 ]    TTCTTCAAATTGAGCCTCAGATGCAG>
            |||||||||| ||||| |||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

27. DNA32_7.     40        50
[   92 ]    TTCTTAAATTGGAGCCCCAGATGCAG>
            ||||| || ||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG

28. DNA32_8.     40        50
[   92 ]    TTCTTAAATTGGAGCCCCAGATGCAG>
            ||||| || ||||||||||||||||||
MSRVqPCR p  TTCTTCAAATGGAGCCCCAGATGCAG
```

Figure S2: Phylogenetic tree representation of aligned clones with related HERV-W and distant HERV-K env gene sequences:

Figure S2A: RNA and DNA clones from BD

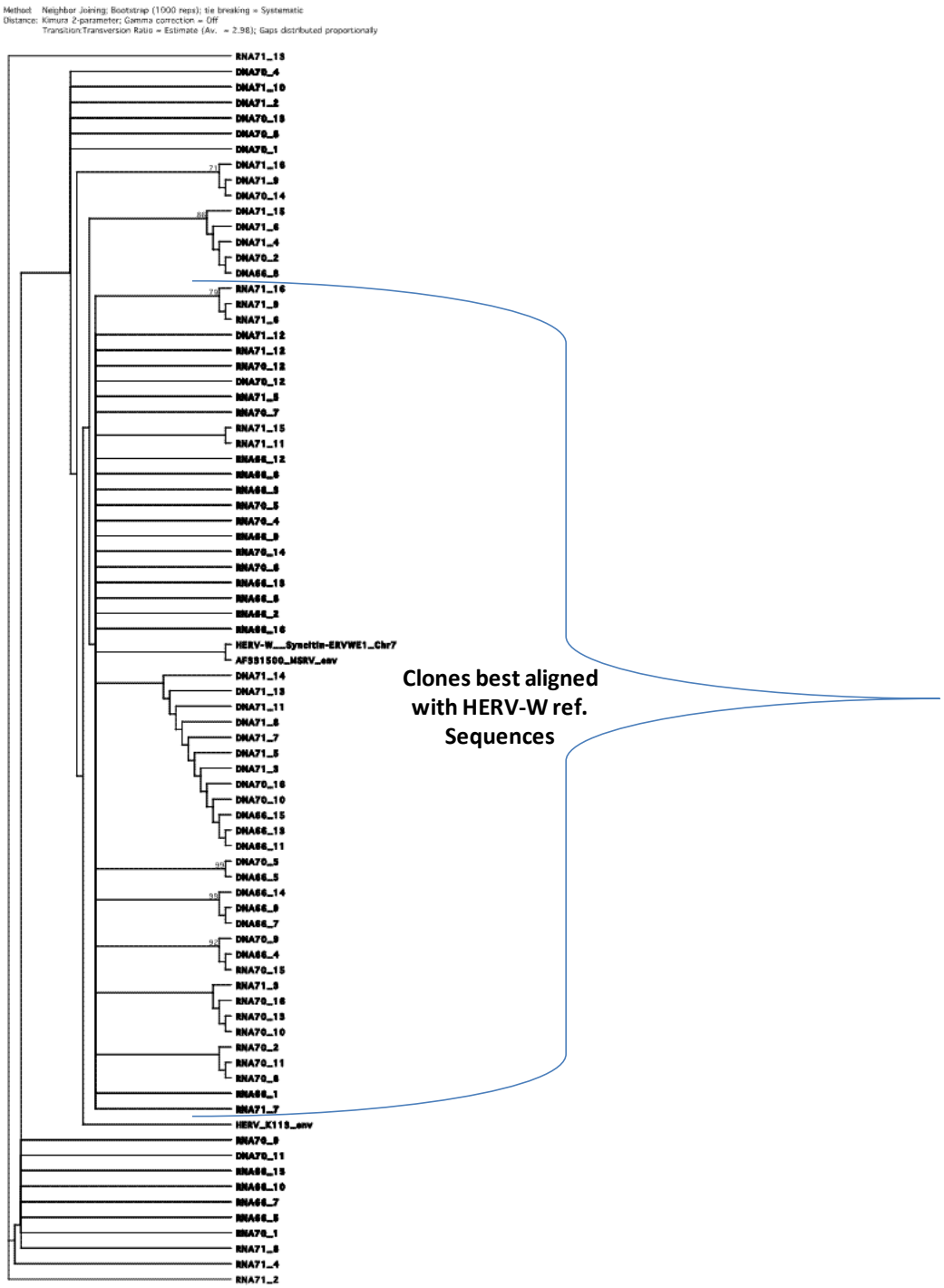

Figure S2B: RNA and DNA clones from SZ

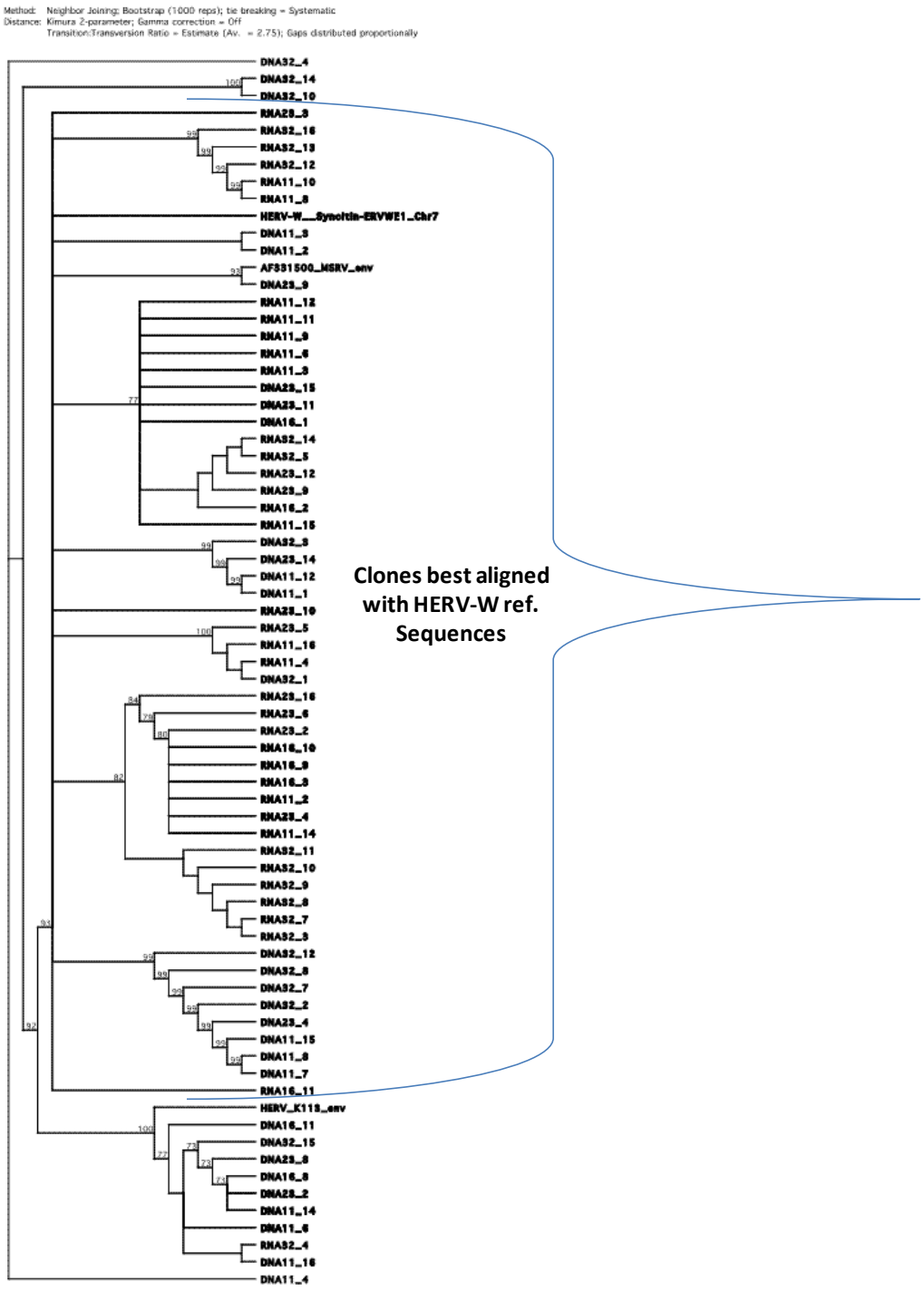

Figure S2C: RNA and DNA clones from HC